Complete Summary

GUIDELINE TITLE

Screening test to detect Chlamydia trachomatis and Neisseria gonorrhoeae infections -- 2002.

BIBLIOGRAPHIC SOURCE(S)

Johnson RE, Newhall WJ, Papp JR, Knapp JS, Black CM, Gift TL, Steece R, Markowitz LE, Devine OJ, Walsh CM, Wang S, Gunter DC, Irwin KL, DeLisle S, Berman SM. Screening tests to detect Chlamydia trachomatis and Neisseria gonorrhoeae infections--2002. MMWR Recomm Rep 2002 Oct 18;51(RR-15):1-38. [160 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Recommendations for the prevention and management of Chlamydia trachomatis infections, 1993. MMWR 1993;42(No. RR-12):1-39.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

- Chlamydia trachomatis infection
- Neisseria gonorrhoeae infection

GUIDELINE CATEGORY

Prevention
Screening

CLINICAL SPECIALTY

Dermatology
Family Practice
Infectious Diseases
Internal Medicine
Obstetrics and Gynecology
Pathology
Pediatrics
Preventive Medicine

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Clinical Laboratory Personnel
Nurses
Physician Assistants
Physicians
Public Health Departments

GUIDELINE OBJECTIVE(S)

- To update the 1993 guidelines for the prevention and management of Chlamydia trachomatis (C. trachomatis) infections (MMWR 1993;42[No. RR-12]:1-39)
- To assist laboratorians, clinicians, and managers:
    - Select screening tests for C. trachomatis or Neisseria gonorrhoeae (N. gonorrhoeae) from the complex array of tests available
    - Establish standard operating procedures for collecting, processing, and analyzing specimens
    - Interpret test results for laboratory reporting, counseling, and treating patients

TARGET POPULATION

- Sexually active men and women in the United States
- Adult and pediatric victims of possible sexual assault or abuse

INTERVENTIONS AND PRACTICES CONSIDERED

1. Laboratory-based tests
    - Culture tests for Chlamydia trachomatis (C. trachomatis) and Neisseria gonorrhoeae (N. gonorrhoeae)
    - Nucleic acid amplification tests (NAATs) for C. trachomatis and N. gonorrhoeae
    - Nucleic acid hybridization and transformation tests for C. trachomatis and N. gonorrhoeae

    - Enzyme immunoassays (EIAs) for C. trachomatis and N. gonorrhoeae
    - Direct fluorescent antibody (DFA) tests for for C. trachomatis
2. Point-of-care tests
    - Gram-stained smear for N. gonorrhoeae
    - Solid-phase enzyme immunoassays and a solid-phase optical immunoassay for C. trachomatis.
3. Additional testing after a positive screening test
4. Methods to enhance performance or reduce costs
    - Selective screening to increase the percentage of positive tests
    - Gray-zone testing to improve test performance
    - Pooling specimens to reduce costs
    - Additional testing to improve test specificity
    - Cotesting for C. trachomatis and N. gonorrhoeae to reduce costs
    - Using leukocyte esterase test (LET) to select for C. trachomatis or N. gonorrhoeae tests
5. Methods for collecting, transporting, and storing endocervical, urethral, and urine specimens
6. Test of cure, treatment failure, and antimicrobial resistance
7. Testing specimens related to possible sexual assault or abuse

MAJOR OUTCOMES CONSIDERED

- Sensitivity, specificity, and positive predictive value of screening tests for Chlamydia trachomatis (C. Trachomatis) or Neisseria gonorrhoeae (N. gonorrhoeae)
- Cost, benefits, and adverse effects of screening tests
- Prevalence of Chlamydia trachomatis or Neisseria gonorrhoeae infections
- Complications of untreated infection and ongoing transmission

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The Centers for Disease Control and Prevention (CDC) staff identified pertinent concerns and compiled the related literature published during 1990 or later.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Subjective Review

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Consultants, selected for their expertise or disciplinary and organizational affiliations, reviewed the draft recommendations. These final guidelines are the recommendations of the Centers for Disease Control and Prevention (CDC) staff who considered contributions from scientific consultants.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Screening

In this report, screening refers to testing persons in the absence of symptoms or signs indicating Chlamydia trachomatis (C. trachomatis) or Neisseria gonorrhoeae (N. gonorrhoeae) infection.

Testing Technologies

Technologies now available for laboratory diagnosis of C. trachomatis and N. gonorrhoeae infections are subdivided into those that are designed for 1) batch

testing in a laboratory or 2) point-of-care testing as single tests or a limited number of tests performed while patients await results. Laboratory-based tests include culture, nucleic acid amplification tests (NAATs), nucleic acid hybridization and transformation tests, enzyme immunoassays (EIAs), and direct fluorescent antibody (DFA) tests. Point-of-care tests have long included the Gram-stained smear for N. gonorrhoeae. Point-of-care tests for C. trachomatis include solid-phase EIAs and a solid-phase optical immunoassay. The leukocyte esterase test (LET) is a dipstick test that is applied to urine specimens to screen for urinary tract inflammation.

Selecting Screening Tests

Multiple considerations affect the selection of a screening test. Test sensitivity is emphasized to minimize occurrence of false-negative tests, which can result in complications of untreated infection and ongoing transmission. However, additional considerations might lead to the selection of a different test (see below, "Additional Considerations in Selecting a Screening Test"). For example, a goal of maximizing test sensitivity to avoid missing the opportunity to treat infected persons might warrant tolerating a limited number of false-positive diagnoses. However, consideration must also be given to reducing the rate and consequences of false-positive tests and to cost (see below, "Methods to Enhance Performance or Reduce Costs"). This report focuses on screening applications of tests for C. trachomatis and N. gonorrhoeae infections. This report also contains a listing of additional indications for C. trachomatis testing and recommendations for choice of test and type of specimen (refer to the original guideline document, Appendix A, "Indications for Chlamydia trachomatis Testing and Test Selection by Specimen Type"); similar information for N. gonorrhoeae is also included (refer to the original guideline document, Appendix B, "Indications for Neisseria gonorrhoeae Testing and Test Selection by Specimen Type").

Performance Perspective for Selecting Screening Tests

On the basis of sensitivity, ease of specimen collection, and ability to assess antimicrobial susceptibility (N. gonorrhoeae), recommendations for screening women and men for C. trachomatis and N. gonorrhoeae genitourinary tract infections are outlined in this section. Recommended screening tests will, compared with less sensitive tests, minimize the risk for disease sequelae and continued transmission of infections as a result of false-negative screening tests. Clinicians should be aware of the potential for adverse consequences caused by a false-positive test result (e.g., substantial psychosocial or legal consequences); patients with positive results should be counseled regarding the potential for false-positive results, and additional testing should be considered. Because such a result might itself be falsely negative and therapies for C. trachomatis and N. gonorrhoeae are safe and effective, treatment might be offered while awaiting results from additional testing or even if an additional test is negative. At lower prevalences, consideration should be given to routine additional testing after a positive screening test. Testing strategies have been proposed that can increase specificity and constrain costs by combining use of NAATs and non-NAATs. A particularly promising strategy called gray-zone testing involves screening with a non-NAAT and using a lower cutoff value than that established by the manufacturer as a criterion for a positive result. A NAAT is then performed as an additional test when the non-NAAT screening test results are in a zone above the

new cutoff value. This strategy could achieve greater sensitivity than would be provided by using a non-NAAT by itself and greater specificity than would be provided by the separate use of either a non-NAAT or a NAAT, and cost less than using a NAAT by itself. This strategy might be useful for screening among lower prevalence populations for which both positive predictive value (PPV) and cost of detecting an infection are of increased concern. This strategy warrants further evaluation (see below, "Additional Considerations in Selecting a Screening Test" and also, "Methods To Enhance Performance or Reduce Costs").

Screening Women for C. trachomatis and N. gonorrhoeae Genitourinary Tract Infections

Tests Used for Screening Women for Genitourinary Tract Infection

Chlamydia trachomatis

- A nucleic acid amplification test (NAAT) performed on an endocervical swab specimen, if a pelvic examination is acceptable; otherwise, a NAAT performed on urine.
- An unamplified nucleic acid hybridization test, an enzyme immunoassay, or direct fluorescent antibody test performed on an endocervical swab specimen.
- Culture performed on an endocervical swab specimen.

Neisseria gonorrhoeae

- Culture performed on an endocervical swab specimen. If transport and storage conditions are not conducive to maintaining the viability of N. gonorrhoeae, a NAAT or nucleic acid hybridization test can be performed on an endocervical swab specimen.
- A NAAT performed on urine.

Screening Men for C. trachomatis and N. gonorrhoeae Urethral Infections

Tests Used for Screening Men for Urethral Infection

Chlamydia trachomatis

- A nucleic acid amplification test (NAAT) performed on an intraurethral swab specimen if collecting such a specimen is acceptable; otherwise, a NAAT performed on urine.
- A non-NAAT or culture performed on an intraurethral swab specimen.

Neisseria gonorrhoeae

- Culture performed on an intraurethral swab specimen if collecting such a specimen is acceptable and transport and storage conditions are suitable for culture.
- A NAAT or nucleic acid hybridization test performed on an intraurethral swab specimen if collecting such a specimen is acceptable; otherwise, a NAAT performed on urine.

Screening Women or Men with Possible Rectal or Pharyngeal Exposure to C. trachomatis or N. gonorrhoeae Infection

Tests for Screening Women or Men for Rectal or Pharyngeal Infection

Chlamydia trachomatis

- Culture performed on rectal or pharyngeal swab specimens; a C. trachomatis-major outer membrane protein (MOMP)-specific stain should be used.
- Direct fluorescent antibody test performed on rectal or pharyngeal swab specimens; a C. trachomatis-MOMP-specific stain should be used.

Neisseria gonorrhoeae

- Culture performed on rectal or pharyngeal swab specimens; a selective medium should be used with additional testing on colonies of typical oxidase-positive, Gram-negative diplococci.

Additional Considerations in Selecting a Screening Test

In addition to test sensitivity, ease of specimen collection, and assessment for antimicrobial susceptibility (N. gonorrhoeae), other considerations in choosing a screening test include 1) the relatively high cost of NAATs (i.e., economic considerations); 2) laboratory environmental changes necessary to implement NAATs; 3) the need for additional testing to support C. trachomatis or N. gonorrhoeae diagnoses; and 4) the likelihood of screening-test-positive persons returning for treatment. The ability of some tests to detect C. trachomatis and N. gonorrhoeae in the same specimen might also affect the choice of test (see below "Methods to Enhance Performance or Reduce Costs"). Recommendations for transporting and storing specimens must also be considered (refer to Appendix D of the original guideline document, "Recommendations for Transport and Storage of Specimens for Chlamydia trachomatis and Neisseria gonorrhoeae Testing, by Testing Procedure Type").

Refer to the original guideline document for further discussion of economic considerations and laboratory environmental changes necessary to implement NAATs.

Need for Additional Testing to Support C. trachomatis or N. gonorrhoeae Diagnoses

Efforts to maximize test sensitivity to avoid missing the opportunity to identify and treat infected persons might warrant tolerating a certain number of false-positive diagnoses. However, consideration must also be given to reducing the rate and consequences of false-positive tests. All tests, including culture for C. trachomatis, occasionally generate false-positive results. For these reasons, all positive tests are considered to be presumptive evidence of infection.

Additional Testing and Patient Management After a Positive Screening Test

- All positive screening tests should be considered presumptive evidence of infection.
- An additional test should be considered after a positive screening test if a false-positive screening test would result in substantial adverse medical, social, or psychological impact for a patient.
- Consideration should be given to routinely performing an additional test after a positive screening test if the positive predictive value is considered low (e.g., <90%).
- Patients should be counseled regarding prompt treatment after a positive screening test because an additional test might be falsely negative.

Consideration of Point-of-Care Testing

Point-of-care tests for C. trachomatis screening are less sensitive than laboratory-based tests but should be considered in situations where screening-test-positive persons might fail to return for treatment or return after substantial delays. Point-of-care tests are not a cost-effective option if they are processed after the patient visit because they are relatively insensitive and require labor-intensive processing. Each health-care provider needs to compare the sensitivities, costs, and treatment rates for point-of-care and laboratory-based tests. Providers need to determine whether the opportunity to provide treatment to certain patients who would otherwise go untreated warrants the additional cost and less favorable sensitivity of point-of-care testing. Food and Drug Administration (FDA)-cleared C. trachomatis and N. gonorrhoeae tests that can be performed rapidly enough to qualify as point-of-care tests must be performed in a Clinical Laboratory Improvement Amendments of 1988 (CLIA)-certified laboratory because they are classified under CLIA as moderate complexity tests.

Methods To Enhance Performance or Reduce Costs

Different approaches have been used to increase the efficiency of standard screening methods. Although selective screening is not a laboratory method, using selective screening criteria is included because the predictive values and cost to detect an infection are strongly influenced by infection prevalence. Another approach is to use a NAAT to test specimens that yield results from an EIA or unamplified nucleic acid probe test that fall in a zone around the cutoff (i.e., gray zone). This technique warrants further evaluation as a method to decrease the gap in sensitivity between NAATs and other tests without incurring the full additional cost of testing all specimens with a NAAT. Interest in pooling specimens for testing by a NAAT is similarly motivated. Augmenting screening tests with additional testing to improve test specificity is of increasing importance because C. trachomatis and N. gonorrhoeae prevalences have declined after the introduction of screening programs and because C. trachomatis screening has expanded into lower prevalence populations. Using test formats (e.g., nucleic acid probe tests or NAATs) that permit testing for both C. trachomatis and N. gonorrhoeae might reduce costs. Finally, the urine leukocyte esterase test, which has a low sensitivity but is inexpensive, has been used to select specimens for testing with a specific C. trachomatis or N. gonorrhoeae test when use of a more sensitive initial test was not feasible.

Refer to the original guideline document for further discussion of: 1) selective screening to increase the percentage of positive tests; 2) gray-zone testing to improve test performance; and 3) pooling specimens to reduce costs.

Additional Testing To Improve Test Specificity

An additional test might be indicated for a person with a positive screening test result, if a false-positive result would have a serious adverse consequence (see above, "Additional Testing and Patient Management After a Positive Screening Test"). Because treatments for C. trachomatis and N. gonorrhoeae are safe and relatively inexpensive, the person might wish to receive and complete treatment while additional testing is being done, or even if the additional test is negative. Routine additional testing to improve the predictive value of a positive screening test should be considered when the prevalence of either C. trachomatis or N. gonorrhoeae infection is low, resulting in a low PPV (e.g., <90%) (see "C. trachomatis and N. gonorrhoeae Test Performance When Used for Screening" and also, "Additional Considerations in Selecting a Screening Test").

Approaches to detect false-positive results by applying an additional test can be ordered by preference on the basis of theoretical considerations.

Approaches to Additional Testing, in Order by Theoretical Consideration, After a Positive Screening Test

- Test a second specimen with a different test that uses a different target, antigen, or phenotype and a different format.
- Test the original specimen with a different test that uses a different target, antigen, or phenotype and a different format.
- Repeat the original test on the original specimen with a blocking antibody or competitive probe.
- Repeat the original test on the original specimen.

Additional Testing After a Positive Chlamydia trachomatis Screening Test

Positive Nonnucleic Acid Amplification Tests (Non-NAAT)

- Culture with a C. trachomatis-specific anti-MOMP (major outer membrane protein) stain can be used after a positive non-NAAT because of the high specificity and the flexibility for additional testing, but culture poses increased difficulties in specimen transport and storage.
- Competitive probe and blocking antibody formats can be used after positive nucleic acid probe tests and enzyme immunoassays, respectively, but this approach is less likely, theoretically, to detect a false-positive result.
- A NAAT has high potential as an additional test after non-NAAT tests because of the increased sensitivity; however, this use of NAATs has received limited evaluation.

Positive NAAT

- Only another NAAT has a sufficiently high sensitivity to serve as an additional test after a positive NAAT; however, such an approach to additional testing has received limited evaluation.

Additional Testing After a Positive Neisseria gonorrhoeae Screening Test

Presumptively Positive Culture

- Acid production from carbohydrates or the Gen-Probe AccuProbe ® or PACE 2 ® tests are the preferred methods to confirm that typical, Gram-negative, oxidase-positive colonies are N. gonorrhoeae.
- Requiring that both the acid production and nucleic acid probe methods be positive for N. gonorrhoeae ensures a high specificity.

Positive Nonculture Test

- Culture with confirmation as described previously is the preferred additional test after a positive nonculture test if specimen transport and storage conditions are suitable.
- A competitive probe format might be used after a positive nucleic acid probe test, but this approach is less likely, theoretically, to detect a false-positive result.
- A NAAT as an additional test after a nonculture test has received limited evaluation, and certain NAATs might cross-react with nongonococcal Neisseria species.

Cotesting for C. trachomatis and N. gonorrhoeae To Reduce Costs

Multiple tests permit testing for both organisms by using the same specimen. The prevalence of N. gonorrhoeae is less than C. trachomatis in the majority of areas of the United States; however, the prevalence of each varies widely, even within such limited areas as cities or counties. Usually, screening for N. gonorrhoeae will not be justified unless screening for C. trachomatis is also warranted. Decisions regarding screening for either or both organisms should not be made without a careful evaluation of the local epidemiology of N. gonorrhoeae and C. trachomatis.

Cotesting for C. trachomatis and N. gonorrhoeae by using tests specially designed for such cotesting should be considered, if transport conditions would reduce the sensitivity of N. gonorrhoeae culture or if using such tests reduces the cost. However, provision should be made to perform an additional test to improve test specificity whenever indicated (see "Additional Testing To Improve Test Specificity") and to obtain isolates for antimicrobial susceptibility testing in the case of a repeated treatment failure (see "Test of Cure, Treatment Failure, and Antimicrobial Resistance" in the original guideline document).

Using Leukocyte Esterase Test (LET) to Select for C. trachomatis or N. gonorrhoeae Tests

LET, which has a low sensitivity but is inexpensive, has been used to select specimens for testing with a specific C. trachomatis or N. gonorrhoeae test when universal testing with a more sensitive initial test is not feasible. Because the test

does not detect either C. trachomatis or N. gonorrhoeae, but rather nonspecific inflammatory enzymes, a positive LET should be followed by specific tests for C. trachomatis and N. gonorrhoeae. The importance of a positive LET that is followed by negative tests for C. trachomatis and N. gonorrhoeae is unknown, but could indicate infection with other organisms (e.g., Trichomonas vaginalis, Ureaplasma urealyticum, or Mycoplasma genitalium).

Collecting, Transporting, and Storing Specimens

Correct specimen collection and handling techniques are critical for all methods used to identify C. trachomatis and N. gonorrhoeae. Even diagnostic tests with the highest performance characteristics cannot produce accurate results when specimens submitted to the laboratory are incorrectly collected. Recommendations for transporting and storing specimens are summarized in Appendix D of the original guideline document.

Collecting and Transporting Specimens for Screening

Specimen Collection Recommendations Applicable to Culture and Nonculture Tests

Although the requirement for columnar endocervical cells applies less to N. gonorrhoeae than to C. trachomatis, guidelines included in this report are appropriate for both organisms.

Specimen-Collection Guidelines

Endocervical Specimens

- Nonculture specimens should be obtained as directed by the test manufacturer in the package insert.
- By established practice, specimens for C. trachomatis tests are obtained after specimens for Gram-stained smear or N. gonorrhoeae culture. When a Papanicolaou smear is to be collected, whether specimens for C. trachomatis or N. gonorrhoeae should be collected first or last is unknown. Bleeding can occur when a Papanicolaou smear is obtained first, and gross blood interferes with certain tests for C. trachomatis and N. gonorrhoeae.
- Before obtaining a specimen, a sponge or large swab should be used to remove all secretions and discharge from the cervical os.
- For nonculture tests, the swab supplied or specified by the test manufacturer should be used.
- The appropriate swab or endocervical brush should be inserted 1-2 cm into the endocervical canal (i.e., past the squamocolumnar junction). The swab should be rotated against the wall of the endocervical canal $\geq$2 times or for the period of time recommended by the manufacturer. The swab should be withdrawn without touching any vaginal surfaces and placed in the appropriate transport medium.

Urethral Specimens

- Specimens should be obtained as directed by the test manufacturer in the package insert.
- If possible, obtaining specimens should be delayed until ≥1 hour after the patient has voided.
- Specimens should be obtained for C. trachomatis tests after obtaining specimens for a Gram-stained smear or N. gonorrhoeae culture.
- For nonculture tests, the swab supplied or specified by the manufacturer should be used.
- The urogenital swab should be inserted gently into the urethra (females, 1-2 cm; males, 2-4 cm). The swab should be rotated in one direction for ≥1 revolutions and withdrawn. For males or females with urethral discharge, exudate collected from the urethral meatus is sufficient for N. gonorrhoeae culture. An intraurethral specimen is required for C. trachomatis testing, regardless of the presence of exudate at the meatus.

Urine Specimens

- Specimens should be obtained as directed by the test manufacturer in the package insert.
- If possible, specimen collection should be delayed until ≥1 hour after the patient has voided.
- First-catch urine (e.g., the first 10-30 cc voided after initiating the stream) should be used.

Sexual Assault and Sexual Abuse

General Guidelines for Testing Specimens Related to Possible Sexual Assault or Abuse

- Endocervical specimens are appropriate for diagnosing C. trachomatis and N. gonorrhoeae infection of sexually active females. However, the immature vaginal epithelium of prepubescent females might be infected, and specimens can be taken from the vagina of these patients.
- Culture is the recommended method for detecting C. trachomatis in urogenital, pharyngeal, and rectal specimens.
    - Only cell culture using standard methods that employ C. trachomatis-specific antibodies to detect intracytoplasmic inclusions should be used.
    - Nonculture/nonamplification tests for C. trachomatis are not sufficiently sensitive and specific for them to be used among either victims or alleged assailants implicated in a sexual assault.
    - Data, experience, and court cases are insufficient to assess the applicability of NAATs to detect C. trachomatis or N. gonorrhoeae in investigating sexual assault and abuse. However, certain researchers have indicated that NAATs for C. trachomatis could be used as an alternative to cell culture if cell culture is unavailable and if another NAAT that targets a different sequence can be performed as an additional test if the initial NAAT test is positive.
- Culture is the recommended method for detecting N. gonorrhoeae in urogenital, pharyngeal, or rectal swab specimens.
    - Gram-negative diplococci isolated on gonococcal selective medium from vaginal, pharyngeal, or rectal specimens must be identified by

the methods described previously (see "Additional Testing After a Positive N. gonorrhoeae Screening Test") to obtain a confirmed identification.
    - Nonculture tests for N. gonorrhoeae are not sufficiently sensitive and specific for them to be used among either victims or alleged assailants implicated in sexual assaults.
    - Gram-stained smear of swab specimens should not be used to detect N. gonorrhoeae among victims of sexual assault or abuse.
- All specimens and isolates from both suspected victims and alleged assailants should be stored at ≤-70 Âº C in the event additional testing is needed.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not specifically stated for each recommendation. The guidelines were developed through literature reviews and extended consultation with non-Centers for Disease Control and Prevention (CDC) sexually transmitted disease (STD) specialists.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Assistance for laboratorians, clinicians, and managers in selecting appropriate screening tests for Chlamydia trachomatis (C. trachomatis) or Neisseria gonorrhoeae (N. gonorrhoeae); establishing standard operating procedures for collecting, processing, and analyzing specimens; and interpreting test results for laboratory reporting, counseling, and treating patients.
- Decreased risk for disease sequelae and continued transmission of infections
- Cost-effective screening

POTENTIAL HARMS

- False-negative screening test results can result in complications of untreated infection and ongoing transmission.
- False-positive screening test results can result in substantial psychosocial or legal consequences.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

These guidelines do not address trachoma and lymphogranuloma venereum, which rarely occur in the United States.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Laboratory Implementation of Nucleic Acid Amplification Tests

Nucleic acid amplification tests (NAATs) require more attention to procedural details and development and maintenance of quality control systems than other nonculture screening tests (e.g., enzyme immunoassays [EIAs] and nonamplified nucleic acid hybridization assays). An increase in such requirements results from the susceptibility of NAAT enzymes to inhibition and the potential of NAATs to generate cross-contaminating target and to detect limited quantities of target present as a contaminant. Despite close attention to quality control, concerns regarding consistency of test performance and reproducibility persist, as indicated by reports of heterogeneity of results in clinical trials and varying rates of reproducing positive results.

As laboratories and health-care providers transition to amplification tests, certain critical concerns should be addressed, including:

- Clinician training whenever a change occurs in the testing method. Training should address:
    - Indications for test use (e.g., appropriate types of specimens)
    - General instruction in obtaining adequate specimens from any site and specific instruction in obtaining a proper endocervical specimen (i.e., one that contains endocervical cells rather than ectocervical cells or vaginal material)
    - Requirements for storage and transport
    - Interpretation of test results
- Monitoring of specimen collection and transport and periodic reinforcement of staff training
- Development of standard laboratory operating procedures and quality-assurance protocols based on package inserts and any supplementary manufacturer instructions. Procedures and protocols should address:
    - Adoption of prescribed work areas and specimen handling procedures to avoid cross-contamination, which is of heightened importance because of the inherent sensitivity of amplification tests
    - Use of positive and negative controls, including a positive control from culture stock or known positive clinical specimens in addition to the control provided in the commercial kit
    - Trade-offs of using amplification controls to identify inhibitors (e.g., reducing false-negative results but decreasing throughput)
    - Creation of a data system that alerts laboratorians when a run includes an unusual number of positive specimens or when positive specimens are clustered within a run.
- Manufacturer-based training of laboratory staff with periodic retraining.
- Clinical Laboratory Improvement Amendments of 1988 (CLIA) requirements for verifying or establishing test performance characteristics. If a laboratory is adopting a Food and Drug Administration (FDA)-cleared test that is classified under CLIA as a high-complexity test, CLIA requires conducting a study to verify that the test performs according to the manufacturer's package insert claims. If the laboratory is adopting a test that has not been cleared by the

FDA or is adopting a modification of a FDA-cleared test, CLIA requires a more extensive study to establish performance specifications, because the FDA-cleared package insert specifications are lacking (Refer to the original guideline document, Appendix C, "Conducting Studies to Evaluate Chlamydia trachomatis and Neisseria gonorrhoeae Tests, Including Studies Required by the Regulations of the Clinical Laboratory Improvement Amendments of 1988 for Verifying or Establishing Test Performance Characteristics").

- Participation in a proficiency testing program.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Johnson RE, Newhall WJ, Papp JR, Knapp JS, Black CM, Gift TL, Steece R, Markowitz LE, Devine OJ, Walsh CM, Wang S, Gunter DC, Irwin KL, DeLisle S, Berman SM. Screening tests to detect Chlamydia trachomatis and Neisseria gonorrhoeae infections--2002. MMWR Recomm Rep 2002 Oct 18;51(RR-15):1-38. [160 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2002 Oct

GUIDELINE DEVELOPER(S)

Centers for Disease Control and Prevention - Federal Government Agency [U.S.]

SOURCE(S) OF FUNDING

United States Government

GUIDELINE COMMITTEE

Not stated

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Report Prepared by: Robert E. Johnson, M.D.; Wilbert J. Newhall, Ph.D.; John R. Papp, Ph.D.; Joan S. Knapp, Ph.D.; Carolyn M. Black, Ph.D.; Thomas L. Gift, Ph.D.; Richard Steece, Ph.D.; Lauri E. Markowitz, M.D.; Owen J. Devine, Ph.D.; Cathleen M. Walsh, Dr.P.H.; Susan Wang, M.D.; Dorothy C. Gunter, M.P.H.; Kathleen L. Irwin, M.D.; Susan DeLisle, M.P.H.; Stuart M. Berman, M.D.

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Recommendations for the prevention and management of Chlamydia trachomatis infections, 1993. MMWR 1993;42(No. RR-12):1-39.

GUIDELINE AVAILABILITY

Electronic copies: Available from the Centers for Disease Control and Prevention (CDC) Web site:

- HTML Format
- Portable Document Format (PDF)

Print copies: Available from the Centers for Disease Control and Prevention, MMWR, Atlanta, GA 30333. Additional copies can be purchased from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402-9325; (202) 783-3238.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

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